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Received for review March 22, 1982. Accepted December 8, 1982.

# Studies on Nitrile Imines. Synthesis of Some Novel Five-Membered Heterocyclic Compounds

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**A variety of new *C*-acetyl and *C*-ethoxycarbonyl derivatives of hydrazonyl bromides have been prepared and reacted with a range of $\alpha,\beta$-unsaturated carbonyl compounds, indene, isothiocyanate, and acetylacetone to afford a wide variety of novel pyrazoline, thiadiazoline, and pyrazole derivatives in excellent yields. The structural elucidation of the final products is based on spectral and analytical studies.**

The synthesis of heterocyclics has held considerable attention in organic synthesis in recent years (*1-6*). Although a variety of five-membered heterocyclic compounds derived from $\alpha$-chlorobenzylidenephenylhydrazine with various dipolarophiles have been well documented in the literature (*7-9*), cycloaddition reactions of *C*-ethoxycarbonyl and *C*-acetyl derivatives of hydrazonyl bromides particularly with $\alpha,\beta$-unsaturated carbonyl compounds have not been reported so far. In view of the ability of hydrazonyl halides to act as good precursors for generating an active 1,3-dipolar species, i.e., nitrile imine, we have prepared some new *C*-ethoxycarbonyl and *C*-acetyl derivatives of hydrazonyl bromides and utilized them in the cycloaddition (*10*, *11*) with various dipolarophiles in order to prepare the heterocyclic compounds, with a view to reveal their synthetic potentialities.

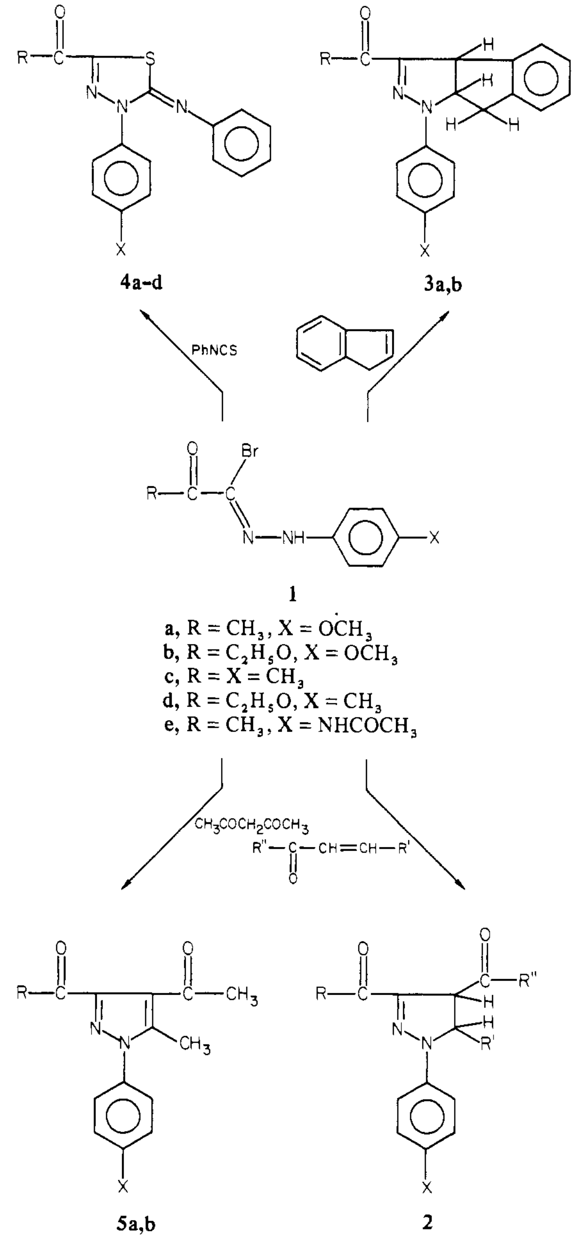
## Experimental Section

All the reagents were obtained from commercial sources (BDH, E. Merck, and S. Merck). Hydrazonyl bromides were prepared according to the method described previously (*12*). Melting points were determined on a Gallenkamp apparatus and are uncorrected. Products were purified by column chromatography over silica gel (60-120 mesh) and purity was checked by TLC. IR spectra were recorded on a Perkin-Elmer infracord spectrophotometer and NMR spectra were taken on a Varian A-90 spectrometer with $Me_4Si$ as an internal standard (Table I). Unless otherwise stated, all the reactions were run under nitrogen atmosphere.

***Preparation of Cycloadducts* (2-4).** To a solution of hydrazonyl bromide (0.005 mol) in dried chloroform (50 mL) was added dipolarophiles in equimolar amounts. The solution was refluxed with constant stirring while triethylamine (0.005 mol) was added dropwise and the solution was allowed to reflux further for 10-12 h. After the mixture was cooled, the solid material was filtered out, washed thoroughly with water, and then dried over sodium sulfate. Chloroform was removed under pressure and the residue on purification followed by crystallization with appropriate solvents (Table II) afforded the desired cycloadducts (**2-4**) in excellent yields (see Scheme I).

***Preparation of Pyrazoles* (5a-b).** To an ethanolic sodium ethoxide or methanolic sodium methoxide solution (prepared

Scheme I



a, $R = CH_3$, $X = OCH_3$
b, $R = C_2H_5O$, $X = OCH_3$
c, $R = X = CH_3$
d, $R = C_2H_5O$, $X = CH_3$
e, $R = CH_3$, $X = NHCOCH_3$

2a(i), $R' = R'' = C_6H_5$
a(ii), $R' = 4\text{-}OCH_3C_6H_4$, $R'' = C_6H_5$
a(iii), $R' = 3,4\text{-}(OCH_3)_2C_6H_3$, $R'' = 4\text{-}OCH_3C_6H_4$
a(iv), $R' = H$, $R'' = NH_2$
b(i), $R' = 3,4\text{-}(OCH_3)_2C_6H_3$, $R'' = 4\text{-}OCH_3C_6H_4$
b(ii), $R' = H$, $R'' = NH_2$
e, $R' = H$, $R'' = NH_2$

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Table I. Spectral Studies of Cycloadducts 2-5

| | $^1$H NMR | | IR (Nujol) | |
|---|---|---|---|---|
| compound no. | $\delta$ | assignment (no. of protons) | $\nu$, cm$^{-1}$ | assignment |
| **2a(i)** | 2.35 (s) | acetyl (3) | 1530 | C=N |
| | 2.51 (s) | methoxy (3) | 1650 | C=O |
| | 4.50 (d, $J = 4.5$ Hz) | methine (1) | 1690 | C=O |
| | 5.80 (d, $J = 4.5$ Hz) | methine (1) | 1600 | C=C |
| | 7.0-8.0 (m) | aromatic (14) | | |
| **2a(ii)** | 2.30 (s) | acetyl (3) | 1510 | C=N |
| | 2.50 (s) | methoxy (3) | 1640 | C=O |
| | 3.46 (s) | methoxy (3) | 1690 | C=O |
| | 6.83-7.96 (m) | aromatic (9) | 1590 | C=C |
| | 4.43 (d, $J = 4.5$ Hz) | methine (1) | | |
| | 5.73 (d, $J = 4.5$ Hz) | methine (1) | 1510 | C=N |
| **2a(iv)** | | | 1640 | C=O |
| | | | 1680 | C=O |
| | | | 3200, 3360 | NH$_2$ |
| **2b(i)** | 2.25 (s) | methoxy (3) | 1590 | C=N |
| | 3.77 (s) | methoxy (3) | 1680 | C=O |
| | 3.84 (s) | methoxy (6) | 1720 | C=O |
| | 1.22 (t, $J = 7.5$ Hz) | methyl (3) | | |
| | 4.14 (q, $J = 7.5$ Hz) | methylene (2) | | |
| | 4.34 (d, $J = 4.5$ Hz) | methine (2) | | |
| | 5.67 (d, $J = 4.5$ Hz) | methine (2) | | |
| | 5.67-7.87 (m) | aromatic (11) | | |
| **2b(ii)** | 1.34 (t, $J = 7.5$ Hz) | methyl (3) | 1550 | C=N |
| | 2.29 (s) | methoxy (3) | 1640 | C=O |
| | 3.22-3.56 (q, $J = 7.5$ Hz) | methylene (2) | 1700 | C=O |
| | 4.16-4.39 (d, $J = 7.5$ Hz) | methylene (2) | 3180, 3360 | NH$_2$ |
| | 4.66-4.92 (q, $J = 7.5$ Hz) | methine (1) | | |
| | 6.79-7.46 (m) | aromatic (4) | | |
| | 7.96 (s) | amino (2) | | |
| **2e** | | | 1500 | C=N |
| | | | 1630 | C=O |
| | | | 1680 | C=O |
| | | | 1570 | C=C |
| | | | 3170, 3360 | NH$_2$ |
| **3a** | | | 1500 | C=N |
| | | | 1640 | C=O |
| | | | 1600 | C=C |
| **3b** | 1.35 (t, $J = 7.5$ Hz) | methyl (3) | 1530 | C=N |
| | 2.33 (s) | methoxy (3) | 1680 | C=O |
| | 3.45 (d, $J = 6.0$ Hz) | methylene (2) | 1600 | C=C |
| | 4.16-4.43 (m) | methylene, methine (3) | | |
| | 6.05 (d, $J = 9$ Hz) | methine (1) | | |
| | 7.1-7.4 (m) | aromatic (8) | | |
| **4a** | | | 1525 | C=N |
| | | | 1640 | C=O |
| | | | 1590 | C=C |
| **4b** | 1.22 (t, $J = 7.5$ Hz) | methyl (3) | 1525 | C=N |
| | 2.46 (s) | methoxy (3) | 1730 | C=O |
| | 4.31 (q, $J = 7.5$, Hz) | methylene (2) | 1590 | C=C |
| | 7.26-7.89 (m) | aromatic (9) | | |
| **4c** | 2.33 (s) | methyl (3) | 1525 | C=N |
| | 2.53 (s) | acetyl (3) | 1645 | C=O |
| | 7.1-7.4 (m) | aromatic (9) | 1590 | C=C |
| **4d** | 1.30 (t, $J = 7.5$ Hz) | methyl (3) | 1530 | C=N |
| | 2.50 (s) | methyl (3) | 1735 | C=O |
| | 4.36 (q, $J = 7.5$ Hz) | methylene (2) | 1590 | C=C |
| | 7.33-8.0 | aromatic (9) | | |
| **5a** | 2.43 (s) | methyl (3) | 1510 | C=N |
| | 2.50 (s) | acetyl (3) | 1670 | C=O |
| | 2.63 (s) | acetyl (3) | 1690 | C=O |
| | 2.70 (s) | methoxy (3) | | |
| | 7.33 (s) | aromatic (4) | 1590 | C=C |
| **5b** | 1.45 (t, $J = 7.5$ Hz) | methyl (3) | 1510 | C=N |
| | 2.43 (s) | methyl (3) | 1650 | C=O |
| | 2.45 (s) | acetyl (3) | 1750 | C=O |
| | 2.60 (s) | methoxy (3) | 1610 | C=C |
| | 4.45 (q, $J =$ Hz) | methylene (2) | | |
| | 7.30 (s) | aromatic (1) | | |

Table II. Physical Characterization of Compounds 2-5[a]

| compd no. | crystallizing solvent | mp, °C | yield, % |
|---|---|---|---|
| 1a | ethanol-water | 130-131 | 85 |
| 1b | ethanol | 86-89 | 90 |
| 1c | methanol | 132-133 | 92 |
| 1d | methanol | 90-91 | 89 |
| 1e | acetone | 245-246 | 84 |
| 2a(i) | benzene-hexane | 185-188 | 80 |
| 2a(ii) | ethanol | 178-179 | 78 |
| 2a(iii) | chloroform-methanol | 180-183 | 90 |
| 2a(iv) | acetone | 240-270 | 76 |
| 2b(i) | benzene-PE | 174-177 | 74 |
| 2b(ii) | ethanol | 229 | 82 |
| 2e | acetone | 240-245 | 80 |
| 3a | ethyl acetate-ethanol | 167-170 | 80 |
| 3b | chloroform-methanol | 139-141 | 89 |
| 4a | ethanol | 207-210 | 86 |
| 4b | methanol | 180-182 | 84 |
| 4c | ethanol | 212-213 | 78 |
| 4d | ethanol | 170-172 | 82 |
| 5a | ethanol-water | 89-90 | 89 |
| 5b | ethanol | 126-128 | 79 |

[a] Satisfactory elemental analyses were obtained for all compounds.

from sodium metal (10.005 mol) and 20 mL of alcohol) was added an equimolar amount of acetylacetone, and the solution was stirred for 0.5 h. The hydrazonyl bromides (**1a,b**; 0.005 mol) were then added under ice-cold conditions to the above reaction mixture. Stirring was continued for 2-3 h, during which bromide went into the solution and a solid either precipitated out in the reaction mixture itself or precipitated on slight dilution with water. The solid was filtered out and further recrystallization with alcohol-water afforded the pyrazoles (**5a,b**) in sufficient purity.

## Acknowledgment

We thank the Director, H. B. Technological Institute, Kanpur, for providing facilities.

**Registry No.** **1a**, 84801-68-3; **1b**, 84801-69-4; **1c**, 74519-39-4; **1d**, 58670-19-2; **1e**, 84801-70-7; **2a(i)**, 84801-71-8; **2a(ii)**, 84801-72-9; **2a(iii)**, 84801-73-0; **2a(iv)**, 84801-74-1; **2b(i)**, 84801-75-2; **2b(ii)**, 84801-76-3; **2e**, 84801-77-4; **3a**, 84801-78-5; **3b**, 84801-79-6; **4a**, 84801-80-9; **4b**, 84801-81-0; **4c**, 84801-82-1; **4d**, 84801-83-2; **5a**, 84801-84-3; **5b**, 63514-81-8; chalcone, 94-41-7; 4-methoxychalcone, 959-33-1; 3,4,4′-trimethoxychalcone, 36685-66-2; 2-propenamide, 79-06-1; indene, 95-13-6; phenyl isothiocyanate, 103-72-0; 2,4-pentanedione, 123-54-6.

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Received for review August 5, 1982. Revised manuscript received October 21, 1982. Accepted December 27, 1982. P.P. and P.D.D. thank CSIR, New Delhi, for financial assistance.